

### **Amendments to the Claims:**

This listing of claims will replace all prior listings, and versions, of claims in the application.

### **Listing of Claims**

1. (currently amended) A method of increasing performance gain during treatment of a cognitive deficit associated with a central nervous system disorder or condition in an animal in need of said treatment comprising the steps of:

(a) providing cognitive training to said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with said central nervous system disorder or condition, and

(b) administering to said animal before, during or after cognitive training, a phosphodiesterase inhibitor which enhances CREB pathway function;

wherein rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain ~~is achieved~~ relative to the performance of said cognitive task achieved by training alone.

2. (withdrawn) The method of claim 1 wherein said animal has undergone neuronal stem cell manipulation.

3. (canceled)

4. (previously presented) The method of claim 1 wherein in step b), cognitive training comprises multiple training sessions.

5. (previously presented) The method of claim 4 wherein said phosphodiesterase inhibitor is administered before and during each training session.

6. (original) The method of claim 1 wherein said animal is a mammal.

7. (original) The method of claim 6 wherein said mammal is a human.
8. (previously presented) The method of claim 1 wherein said phosphodiesterase inhibitor induces CREB-dependent gene expression.
9. (withdrawn) The method of claim 8 wherein said augmenting agent up-regulates a positive effector of CREB pathway function.
10. (withdrawn) The method of claim 9 wherein said positive effector of CREB pathway function is a CREB activator.
11. (canceled)
12. (withdrawn) The method of claim 11 wherein said negative effector of CREB pathway function is a CREB repressor.
13. (withdrawn) The method of claim 1 wherein said augmenting agent is a CREB functional modulator.
14. (currently amended) A method of increasing performance gain during enhancement of a specific aspect of cognitive performance in an animal in need thereof comprising the steps of:  
(a) providing cognitive training to said animal under conditions sufficient to produce an improvement in performance of a specified cognitive task by said animal, and  
(b) administering to said animal before, during or after cognitive training, a phosphodiesterase inhibitor which enhances CREB pathway function ;  
wherein rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain ~~is achieved~~ relative to the performance of said specified cognitive task achieved by training alone.

15. (canceled)

16. (original) The method of claim 14 wherein in step b), training comprises multiple training sessions.

17. (previously presented) The method of claim 16 wherein said phosphodiesterase inhibitor is administered before and during each training session.

18. (original) The method of claim 14 wherein said animal is a mammal.

19. (original) The method of claim 18 wherein said mammal is a human.

20. (previously presented) The method of claim 14 wherein said phosphodiesterase inhibitor induces CREB-dependent gene expression.

21. (withdrawn) The method of claim 20 wherein said augmenting agent up-regulates a positive effector of CREB pathway function.

22. (withdrawn) The method of claim 21 wherein said positive effector of CREB pathway function is a CREB activator.

23. (canceled)

24. (withdrawn) The method of claim 23 wherein said negative effector of CREB pathway function is a CREB repressor.

25. (withdrawn) The method of claim 14 wherein said augmenting agent is a CREB functional modulator.

26. (withdrawn) A method of treating a cognitive deficit associated with age-associated memory impairment in an animal in need of said treatment comprising the steps of:

(a) administering to said animal an augmenting agent which enhances CREB pathway function; and

(b) training said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with age-associated memory impairment, whereby said cognitive deficit is treated.

27. (withdrawn) The method of claim 26 wherein a performance gain is achieved relative to the performance of said cognitive task achieved by training alone.

28. (withdrawn) The method of claim 26 wherein in step b), training comprises multiple training sessions.

29. (withdrawn) The method of claim 28 wherein said augmenting agent is administered before and during each training session.

30. (withdrawn) The method of claim 26 wherein said animal is a mammal.

31. (withdrawn) The method of claim 30 wherein said mammal is a human.

32. (withdrawn) The method of claim 26 wherein said augmenting agent induces CREB-dependent gene expression.

33. (withdrawn) A method of treating a cognitive deficit associated with a neurodegenerative disease in an animal in need of said treatment comprising the steps of:

(a) administering to said animal an augmenting agent which enhances CREB pathway function; and

(b) training said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with said neurodegenerative

disease, whereby said cognitive deficit is treated.

34. (withdrawn) The method of claim 33 wherein a performance gain is achieved relative to the performance of said cognitive task achieved by training alone.

35. (withdrawn) The method of claim 33 wherein said neurodegenerative disease is selected from the group consisting of: delirium, dementia, Alzheimer's disease, Parkinson's disease and Huntington's disease.

36. (withdrawn) The method of claim 33 wherein in step b), training comprises multiple training sessions.

37. (withdrawn) The method of claim 36 wherein said augmenting agent is administered before and during each training session.

38. (withdrawn) The method of claim 33 wherein said animal is a mammal.

39. (withdrawn) The method of claim 38 wherein said mammal is a human.

40. (withdrawn) The method of claim 33 wherein said augmenting agent induces CREB-dependent gene expression.

41. (withdrawn) A method of treating a cognitive deficit associated with a psychiatric disease in an animal in need of said treatment comprising the steps of:

(a) administering to said animal an augmenting agent which enhances CREB pathway function; and

(b) training said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with said psychiatric disease, whereby said cognitive deficit is treated.

42. (withdrawn) The method of claim 41 wherein a performance gain is achieved relative to the performance of said cognitive task achieved by training alone.

43. (withdrawn) The method of claim 41 wherein said psychiatric disease is selected from the group consisting of: depression, schizophrenia, autism and attention deficit disorder.

44. (withdrawn) The method of claim 41 wherein in step b), training comprises multiple training sessions.

45. (withdrawn) The method of claim 44 wherein said augmenting agent is administered before and during each training session.

46. (withdrawn) The method of claim 41 wherein said animal is a mammal.

47. (withdrawn) The method of claim 46 wherein said mammal is a human.

48. (withdrawn) The method of claim 41 wherein said augmenting agent induces CREB-dependent gene expression.

49. (currently amended) A method of increasing performance gain in the treatment of a cognitive deficit associated with cerebrovascular disease in an animal in need of said treatment comprising the steps of:

(a) providing cognitive training to said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with said cerebrovascular disease, and

(b) administering to said animal before, during or after cognitive training, a phosphodiesterase inhibitor which enhances CREB pathway function;

wherein rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain is ~~achieved~~ relative to the performance of said cognitive task achieved by training alone.

50. (canceled)

51. (original) The method of claim 49 wherein said cerebrovascular disease is selected from the group consisting of stroke and ischemia.

52. (previously presented) The method of claim 49 wherein in step b), cognitive training comprises multiple training sessions.

53. (previously presented) The method of claim 49 wherein said phosphodiesterase inhibitor is administered before and during each training session.

54. (original) The method of claim 49 wherein said animal is a mammal.

55. (original) The method of claim 54 wherein said mammal is a human.

56. (previously presented) The method of claim 49 wherein said phosphodiesterase inhibitor induces CREB-dependent gene expression.

57. (currently amended) A method of increasing performance gain in the treatment of a cognitive deficit associated with a trauma dependent loss of cognitive function in an animal in need of said treatment comprising the steps of:

(a) providing cognitive training to said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with said trauma dependent loss of cognitive function, and

(b) administering to said animal before, during or after cognitive training, a phosphodiesterase inhibitor which enhances CREB pathway function;

wherein rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain ~~is achieved~~ relative to the performance of said cognitive task achieved by training alone.

58. (canceled)

59. (withdrawn) The method of claim 57 wherein said trauma dependent loss of function is selected from the group consisting of: head trauma and brain trauma.

60. (previously presented) The method of claim 57 wherein in step b), cognitive training comprises multiple training sessions.

61. (previously presented) The method of claim 60 wherein said phosphodiesterase inhibitor is administered before and during each training session.

62. (original) The method of claim 57 wherein said animal is a mammal.

63. (original) The method of claim 62 wherein said mammal is a human.

64. (previously presented) The method of claim 57 wherein said phosphodiesterase inhibitor induces CREB-dependent gene expression.

65. (withdrawn) A method of treating a cognitive deficit associated with a genetic defect in an animal in need of said treatment comprising the steps of:

(a) administering to said animal an augmenting agent which enhances CREB pathway function; and

(b) training said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task associated with said genetic defect, whereby said cognitive deficit is treated.

66. (withdrawn) The method of claim 65 wherein a performance gain is achieved relative to the performance of said cognitive task achieved by training alone.



67. (withdrawn) The method of claim 65 wherein said genetic defect is selected from the group consisting of: Rubinstein-Taybi syndrome and down syndrome.

68. (withdrawn) The method of claim 65 wherein in step b), training comprises multiple training sessions.

69. (withdrawn) The method of claim 68 wherein said augmenting agent is administered before and during each training session.

70. (withdrawn) The method of claim 65 wherein said animal is a mammal.

71. (withdrawn) The method of claim 70 wherein said mammal is a human.

72. (withdrawn) The method of claim 65 wherein said augmenting agent induces CREB-dependent gene expression.

73. (withdrawn) A method of improving learning in an animal with a learning disability comprising the steps of:

(a) administering to said animal an augmenting agent which enhances CREB pathway function; and

(b) training said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with said learning disability, whereby learning is improved.

74. (withdrawn) The method of claim 73 wherein a performance gain is achieved relative to the performance of said cognitive task achieved by training alone.

75. (withdrawn) The method of claim 73 wherein in step b), training comprises multiple training sessions.

76. (withdrawn) The method of claim 75 wherein said augmenting agent is administered before and during each training session.

77. (withdrawn) The method of claim 73 wherein said animal is a mammal.

78. (withdrawn) The method of claim 77 wherein said mammal is a human.

79. (withdrawn) The method of claim 73 wherein said augmenting agent induces CREB-dependent gene expression.

80. (withdrawn) A method for repeated stimulation of neuronal activity or a pattern of neuronal activity in an animal comprising the steps of:

(a) administering to said animal an augmenting agent which enhances CREB pathway function; and

(b) training said animal under conditions sufficient to stimulate neuronal activity or a pattern of neuronal activity in said animal.

81. (withdrawn) The method of claim 80 wherein in step b), training comprises multiple training sessions.

82. (withdrawn) The method of claim 81 wherein said augmenting agent is administered before and during each training session.

83. (withdrawn) The method of claim 80 wherein said animal is a mammal.

84. (withdrawn) The method of claim 83 wherein said mammal is a human.

85. (withdrawn) The method of claim 80 wherein said augmenting agent induces CREB-dependent gene expression.

86. (withdrawn) A method of therapy of a cognitive deficit associated with a central nervous system disorder or condition in an animal having undergone neuronal stem cell manipulation comprising the steps of:

- (a) administering to said animal an augmenting agent which enhances CREB pathway function; and
- (b) training said animal under conditions sufficient to stimulate neuronal activity or a pattern of neuronal activity in said animal.

87. (withdrawn) The method of claim 86 wherein training in step b) further produces an improvement in performance by said animal of a cognitive task whose deficit is associated with said central nervous system disorder or condition.

88. (withdrawn) The method of claim 87 wherein a performance gain is achieved relative to the performance of said cognitive task achieved by training alone.

89. (withdrawn) The method of claim 86 wherein in step b), training comprises multiple training sessions.

90. (withdrawn) The method of claim 89 wherein said augmenting agent is administered before and during each training session.

91. (withdrawn) The method of claim 86 wherein said animal is a mammal.

92. (withdrawn) The method of claim 91 wherein said animal is a human.

93. (withdrawn) The method of claim 86 wherein said augmenting agent induces CREB-dependent gene expression.

94. (canceled)

95. (canceled)

96. (canceled)

97. (canceled)

98. (currently amended) A method of increasing performance gain during rehabilitation of a cognitive deficit associated with a trauma dependent loss of cognitive function from stroke in an animal in need of said rehabilitation comprising the steps of:

(a) providing cognitive training to said animal under conditions sufficient to produce an improvement in performance by said animal of a cognitive task whose deficit is associated with said trauma dependent loss of cognitive function from stroke, and

(b) administering to said animal before, during or after cognitive training, a phosphodiesterase inhibitor which enhances CREB pathway function;

whereby rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain ~~is achieved~~ relative to the performance of said cognitive task achieved by training alone.

99. (canceled)

100. (previously presented) The method of claim 98 wherein in step (b) cognitive training comprises multiple training sessions.

101. (previously presented) The method of claim 98 wherein said phosphodiesterase inhibitor is administered before and during each training session.

102. (previously presented) The method of claim 98 wherein said animal is a mammal.

103. (previously presented) The method of claim 102 wherein said mammal is a human.

104. (previously presented) The method of claim 98 wherein said phosphodiesterase inhibitor induces CREB-dependent gene expression.

105-106. (canceled)